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## **Ultrasonic Doppler Measurement of Renal Artery Blood Flow**

by

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**INTEGRATED CIRCUITS LABORATORY**  
**STANFORD ELECTRONICS LABORATORIES**

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Ames Research Center  
Moffett Field, California 94035

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RENAL ARTERY BLOOD FLOW

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### ABSTRACT

This Annual Report summarizes research completed during the past eleven months -- September 1, 1975 through July 31, 1976. During this period, studies were made of (1) blood flow redistribution during lower body negative pressure (LBNP), (2) the profile of blood flow across the mitral annulus of the heart (both perpendicular and parallel to the commissures), (3) testing and evaluation of a number of pulsed Doppler systems, (4) acute calibration of perivascular Doppler transducers, (5) redesign of the mitral flow transducers to improve reliability and ease of construction, and (6) a frequency offset generator designed for use in distinguishing forward and reverse components of blood flow by producing frequencies above and below the offset frequency. Finally methodology has been developed and initial results have been obtained from a computer analysis of time-varying Doppler spectra.

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## INTRODUCTION

This Report documents research completed under NASA Grant NGR-05-020-615 between August 31, 1975 and August 1, 1976. At this point, substantial progress can be reported in seven of the nine proposed tasks. The work has resulted in a number of papers that have been presented at professional society meetings. The documents relating to these presentations are included as annexes.

The active areas of research concentration during the past year include changes in the pattern of blood flow under the stress of lower body negative pressure (LBNP), the velocity and volume flow in the orifice of canine mitral valves, the evaluation of several Doppler flowmeter systems in terms of their ability to provide useful physiological information, and analysis of the Doppler response spectra by computer to eliminate the effect of heart or blood vessel wall motion on the volume flow estimation. These results are discussed in greater detail below.



## BLOOD FLOW REDISTRIBUTION DURING LOWER BODY NEGATIVE PRESSURE

A means for testing the cardiovascular system under stress is to induce lower-body negative pressure (LBNP) and observe changes in the patterns of blood flow and blood pooling similar to that which occurs under shock. Effective blood flow measurement is required.

The first integrated-circuit, totally-implantable, directional CW Doppler flowmeters, shown in Figure 1, have been used at Ames Research Center to measure blood flow redistribution during LBNP. An LBNP study has been designed involving seven or eight implantations, each consisting of three of these units. Twelve units, each to be recycled on time, are designated for this study.

Two flowmeters were implanted on the mesenteric and iliac arteries, respectively, of a mongrel dog. In addition to the Stanford devices, commercially available flow transducers were placed on the splenic and iliac arteries to allow additional comparisons. An inflatable perivascular occluder was also placed on the iliac artery, distal to the electromagnetic and Doppler flow transducers. This allowed in vivo comparisons between electrical and occlusive flow "zeros." Figure 2 shows the results from the awake, unanesthetized animal one day after surgery. The slight fluctuations for both systems during occlusive zero are produced by surges against the distal occlusion.

The Doppler occlusive and electrical "zeros" were always coincidental, and continue to be so one month after surgery. During LBNP, both iliac and mesenteric flows decreased. At 50 mm Hg LBNP, mean mesenteric flow decreased more than 50% and the phasic waveform showed a conversion from

unidirectional to bidirectional flow. This demonstrates the value and necessity for the use of bidirectional flowmeters when studying dynamic vascular beds. Without this bidirectional capability, reverse flow would have been rectified and mean flow would have been overestimated.

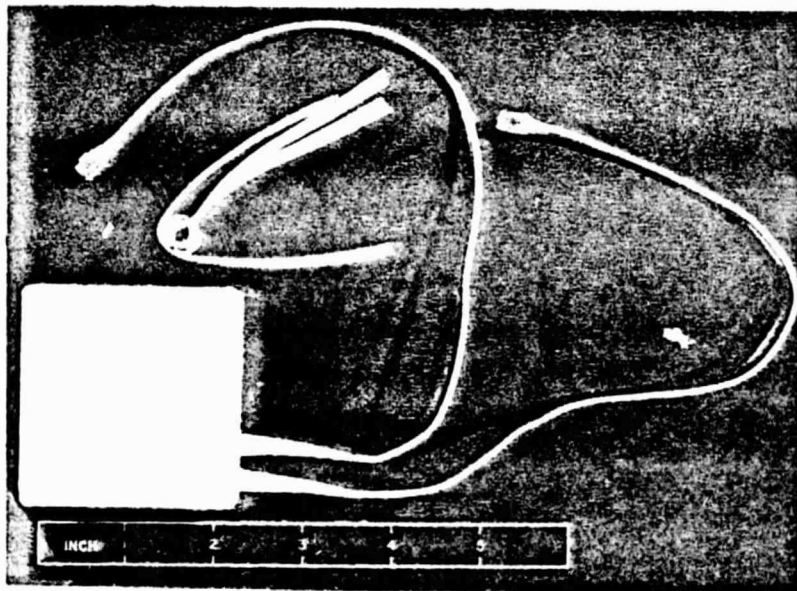


Figure 1. A Totally-Implantable, Directional CW Doppler Blood Flowmeter.



Figure 2. In vivo Comparisons Between Electrical and Occlusive Flow "Zeros" in an Awake, Unanesthetized Animal One Day After Surgery.



The next three flowmeters were implanted on mesenteric, renal, and iliac arteries of another dog and were functional three weeks after implantation, permitting one complete LBNP study. However, they failed immediately thereafter, due to body fluid leakage into the package. Another set, which was implanted before the first set failed, also became inoperative and could not complete a full LBNP study. This leakage problem was totally unexpected because previous packages, with presumably the same design, had withstood several months implantation. The problem has been traced to a package structure which was weakened in the process of accommodating a more reliable battery, which also has a larger diameter. The interim corrective measure is to place the battery in an external package connected by wire to the electronics package. Three packages with this feature have been completed and will be implanted. If this succeeds, the remaining units will be packaged this way and the previous units that failed will be reworked or replaced so that the seven or eight LBNP studies, originally planned, can be completed.

## MITRAL FLOW STUDIES

The initial phase of the mitral flow study has been concluded. Mitral flow information has been collected from seven chronically instrumented dogs with normal valves. The results of this study are being summarized for publication. The Doppler methods used are presented in Annex A. Typical time-varying velocity profiles along the plane of the mitral annulus (normal to the commissures) are shown in Figure 3, along with ECG. They demonstrate the dynamic nature of flow through an orifice of variable dimensions. In contrast, profiles measured along the plane of the annulus, but parallel to the commissures, appear blunt throughout ventricular filling. Initial results from spectral analysis of the CW audio signals are discussed as part of the overall analysis of time-varying Doppler spectra, below. Acute studies evaluating a variety of commercially available, prosthetic valve designs have also been completed and the results will be summarized for publication.

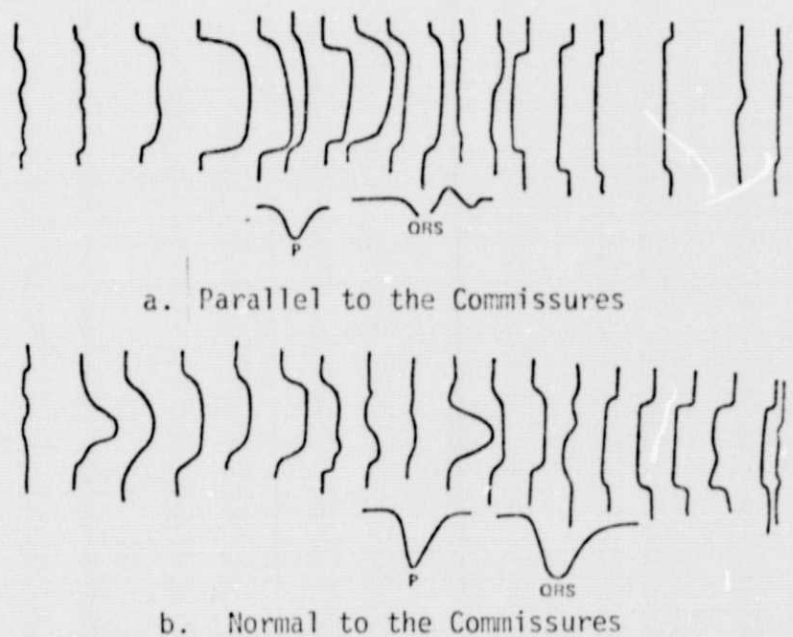


Figure 3. Time-Varying Velocity Profiles in the Plane of the Mitral Annulus

## ACUTE CALIBRATION STUDY

The acute calibration study described in the last report has now been completed. The results are summarized in a paper presented at the May, 1976, International Symposium on Biotelemetry at Asilomar, California, and will be presented, also, at the 29th Annual Conference on Engineering in Medicine and Biology (ACEMB) in Boston in November, 1976. The abstract for the latter presentation is reproduced as Annex C, which gives details of the methods used and results obtained.

## SPECIAL PURPOSE TRANSDUCERS

The design of the mitral flow transducer has been altered significantly during the past year to improve reliability and ease of construction. The piezoelectric elements are now molded into, rather than glued on to, the epoxy pedestals. This affords better mechanical protection and angle control, and reduces assembly time.

The use of commercially available stainless steel cables has greatly extended the useful transducer lifetime. In addition, a new multielement transducer suitable for measurement of mitral or tricuspid flows has been designed for future construction. Due to design similarities, repeated use of the mitral transducers has provided useful information concerning eventual, in vivo failure modes for more conventional CW and pulsed transducer designs.

## FREQUENCY OFFSET GENERATOR

The frequency offset generator has been constructed and awaits testing. With this device, directional audio signals are converted from quadrature to frequency offset formats. Thus, forward and reverse flow components are translated to frequencies which are, respectively, above and below the offset frequency. This technique allows computer analysis (described below) of the directional Doppler spectra from mitral, acute calibration and LBNP studies.

## COMPUTER ANALYSIS OF TIME-VARYING DOPPLER SPECTRA

The methodology and initial results from a computer technique for analysis of time-varying Doppler spectra have been discussed in the last report. This technique has proved useful in the analysis of mitral flow data where simultaneous atrial wall and blood flow signals are present. Unfiltered power spectra from contiguous segments of CW mitral data showed the simultaneous presence of two distinct and widely separated power peaks. Independent analyses confirmed that the low-frequency information was produced by atrial wall motion. Under these conditions, velocity estimations by either zero-crossing or centroid detection schemes would be in error by approximately 50%. The motion signals were present throughout much of the cardiac cycle and often undetectable by ear. After high-pass filtering (800 Hz) and frequency smoothing, the actual flow signal emerged. During the conduit phase of ventricular filling, most of the power was found to be concentrated at one frequency. This implies plug flow within the sample volume which extends 6 cm across the center of the annulus. During atrial contraction (determined by comparison with strip chart information) the power was spread from the 800 Hz high-pass frequency to cover the frequency band to as high as 3 kHz. Conclusions regarding turbulence during this time will be possible following addition of the directional sensing capability provided by the frequency offset generator. These techniques may also prove valuable for the separation of systematic noise from transcutaneous Doppler signals.



## A TECHNIQUE FOR MEASUREMENT OF MITRAL FLOW HEMODYNAMICS IN CHRONICALLY INSTRUMENTED ANIMALS

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Accurate in vivo investigation of mitral flow hemodynamics is technically difficult. Interpretation of Doppler flow data from transcutaneous or epicardial transducers is complicated by motion of the mitral annulus and atrial walls during the cardiac cycle. Catheter tip transducers can provide localized velocity information, but measurements of catheter position, velocity profile and volume flow are difficult to quantitate. Because of these problems, an intra-cardiac Doppler transducer has been employed to allow direct measurement of mitral hemodynamics in chronically instrumented animals. Continuous wave (CW) and pulsed Doppler operation allow measurement of time-varying velocity profiles and vectors at fixed locations above the mitral valve. Spectral analysis of the Doppler audio signal allows estimation of velocity distribution and turbulence within the sample regions.

The transducer is constructed from stainless steel, cast epoxy, and LTZ-2 piezoelectric materials. The three piezoelectric elements are backed with echospheres and coated with a 1/4 wave matching layer for efficient pulsed operation. The elements are then molded onto pedestals displaced by 90° around a stainless steel ring. The completed transducer is implanted in a supra-annular position inside the left atrium. Percutaneous leads pass through the left atrial appendage and are externalized at the base of the neck.

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American Institute of Ultrasound in  
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Sequential pulsed Doppler operation of the elements allows measurement of time-varying velocity profiles along and across the valve commissures. A bidirectional pulsed Doppler flowmeter measures velocities at eight range gated locations across the valve. Velocity profile and ECG signals are multiplexed onto a fiber-optic visicorder which is unblanked at controlled rates to record 12, 24, 48 or 96 profile samples per second. The pulsed echo signal can also be multiplexed with ECG to provide TM-mode records of relative motion between the mitral annulus and atrial walls.

During CW operation, the three non-redundant pairs of elements measure velocity components along separate axes at the valve center. The velocity vector can then be found by triangulation. Alternate multiplexing and transducer schemes allow real time vector determinations at any point in the cardiac cycle.

Use of this technique has allowed precise definition of the instantaneous transmitral flow velocity distribution in the awake, chronically instrumented dog. Similar studies are in progress to evaluate a variety of commercially available, prosthetic mitral valve designs.

## Annex B

### RADIOTELEMETRY OF RENAL AND ILIAC BLOOD FLOW FROM EXERCISING HEART AUTOTRANSPLANT RECIPIENTS

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Previous studies have demonstrated the sustained capacity of the transplanted heart to respond in a directionally appropriate manner to the metabolic demands of exercise (1,2). In comparison to the normal heart, however, the absolute level of cardiac output from the transplanted heart is consistently lower (3). Little information is available to describe the adaptive peripheral circulatory changes which allow normal levels of activity despite reduced cardiac outputs. The purpose of this study was to investigate these adaptations by comparing peripheral flow distribution during rest and exercise in the dog.

#### METHODS

Totally implanted CW Doppler flowmeters (4) were employed to measure blood flow velocities through the renal and iliac arteries of adult mongrel dogs. A total of 16 flowmeters were implanted in 8 animals (5 controls and 3 heart autotransplant recipients) to compare their resting and exercise flow values. The use of totally implanted telemetry systems allowed frequent measurements from the unanesthetized animals without the inconveniences often associated with percutaneous leads.

Flowmeter operation was controlled by a 500 KHz "command transmitter" which activated the implanted circuitry. The transducer elements (1.5 mm square) were operated at an ultrasonic frequency of 6MHz. The Doppler audio signals were telemetered in the 88-108 MHz band to commercial FM receivers. In the absence of interference from adjacent signal sources, telemetry range exceeded 50 meters. The received Doppler audio signals were processed by conventional zero-crossing techniques.

Following a 3 week recovery period, the animals were treadmill exercised (30° incline) in accordance with the protocol developed by Barber, et al. (5). Studies were repeated over a 2 week period to verify consistency of response. Arteriograms were performed prior to recovery of the probes to estimate lumen diameter and verify that the

transducers presented no flow obstruction. Direct bleed-out studies were also performed with 3 animals to verify flow-meter linearity.

## RESULTS

At the time of study, the transplant recipients exhibited characteristics often associated with cardiac denervation i.e. peripheral edema, absence of a startle response, and complete absence of normal sinus arrhythmia (6). For both groups of animals maximum response was achieved after 1 min. of exercise. The hemodynamic findings for normal and transplant recipient animals are summarized in Table 1.

Table 1. Flow and Heart Rate Response to Exercise

	Autotransplant	Normals
RH	56.7(7.4)	108(8)
EH	131.7(27.4)	190(21.1)
RR	45(3.5)	62.7(19.7)
ER	41.7(2.1)	53.8(15.7)
RI	20(0)	33.8(9.2)
EI	69(1.4)	74(18.3)

Numbers in parentheses indicate  $\pm$  S.E.M; RH= Resting heart rate (beats/min); EH= Exercise heart rate (beats/min); RR= Resting mean renal flow velocity (cm/sec); ER= Exercise mean renal flow velocity (cm/sec); RI= Resting mean iliac flow velocity (cm/sec); EI= Exercise mean iliac flow velocity (cm/sec).

In comparison to the normal animals, the absolute levels of heart rate, mean renal and iliac flow velocities were consistently lower for the transplant recipients during rest and exercise. In contrast, however, the relative changes with exercise in heart rate and flow velocities were similar for both groups of animals (see Table 2). For both groups, heart rate approximately doubled, mean iliac flow velocities increased more than two-fold, and mean renal flow velocities decreased by less than 20%.

4. Curtis PJ: Specifications for implantable ultrasonic flowmeters. (Unpublished information)
5. Barger AC, Richards V, Metcalfe J, et al: Regulation of the circulation during exercise. Cardiac output (direct fick) and metabolic adjustments in the normal dog. Am J Physiol 184: 613, 1956
6. Willman VL, et al: Physiologic alterations following transplantation of the heart. Proc 1st Intl Cong Transpl Soc: 661, 1967.

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THEORETICAL AND EXPERIMENTAL ANALYSIS OF THE ACCURACY OF CW  
DOPPLER FLOW MEASUREMENT WITH IMPLANTABLE TRANSDUCERS

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**INTRODUCTION:** During the past decade, numerous investigators have employed continuous wave (CW) Doppler techniques for ultrasonic measurement of blood flow. Although various theoretical and practical aspects of this process have been reported, little published information specifically considers the impact of the perivascular transducer design on measurement accuracy. The purpose of this research was to identify and quantify those effects.

**METHODS:** Studies of the critical interactions between piezoelectric element size and: (1) audio signal-to-noise ratio; (2) geometry of the sample region; and (3) accuracy of center and mean velocity estimations were performed using *in vivo*, *in vitro*, and computer techniques. For the *in vivo* experiments, a short segment of descending thoracic aorta (8 to 12 mm O.D.) of anesthetized dogs was exposed and fitted with adjacent electromagnetic (EM) and Doppler flow transducers (3 mm square elements). The time varying spectral content of the CW Doppler audio signals was determined by a time compression analysis technique. Velocity profiles were measured with a directional pulsed Doppler flowmeter. Synchronized time-varying velocity profiles and ECG were multiplexed onto a fiber-optic oscilloscope recorder. Measured and predicted (1) velocity profiles were compared. Doppler transducers incorporated into the arterial cannula provided experimental control and additional comparisons during stopwatch and beaker calibrations. Hematocrits were also measured. *In vitro* acoustical properties of various coupling materials, freshly excised vessels, and vessel analogs were also examined by pulse echo techniques. Further studies were performed to determine the effects of vessel-cuff misalignment and variations in transducer symmetry on system performance.

**RESULTS:** (1) The audio signal-to-noise ratio increases as the edge length to the third power, for square transducers, with all other factors held constant. (2) For pulsatile flows at a heart rate of 2Hz, the instantaneous velocity profiles were blunt throughout the cardiac cycle. They remained so during direct stopwatch and beaker calibration despite variations in the distal impedance. As heart rate was lowered, the profiles exhibited changes consistent with Womersley's predictions. (3) At a heart rate of 2Hz, the instantaneous Doppler spectra were narrow during pulsatile flow in the intact circulation and direct calibrations. (4) No changes were observed in back-scattered signal levels for physiologic variations in hematocrit (35-45 vol%). (5) Round-trip acoustical loss through the vessel wall was 1.5 db/mm at 6 MHz for both the *in vitro* and *in vivo* cases. (6) Significant (>5%) errors were possible when water-based gels were used for acoustical coupling and the effects of beam diffraction were ignored. (7) The computer results show the overestimation of true flow velocity as a function of both velocity profile and transducer element size. (Fig. 1).

(8) Following normalization for: (a) the size of the piezoelectric elements relative to the lumen, and (b) predicted velocity profiles, the true flow velocities were determined with an accuracy of  $\pm 10\%$ .

**DISCUSSION:** These results indicate a linear, constant relationship between measured velocity and volume flow on straight sections of relatively large vessels such as the descending thoracic aorta. For this case, velocity profiles are blunt and narrow audio spectra are produced, allowing accurate processing by zero-crossing techniques. Determination of lumen diameter allows direct conversions from velocity to volume flow without the necessity for direct calibration. For smaller vessels, such as the renal artery, the velocity profiles become parabolic. Under these conditions, the relationship between mean velocities in the sample region and mean velocity across the vessel must be carefully calculated as a function of element size. Zero-crossing errors due to spectral spreading must also be considered. (Fig. 1). Without consideration of these factors, mean velocity across the vessel may be overestimated by more than 50%, regardless of the signal processing scheme employed.

(1) Womersley, R. An Elastic Tube Theory of Pulse Transmission and Oscillatory Flow in Mammalian Arteries. WADC Tech. Report 56-614, 1957.

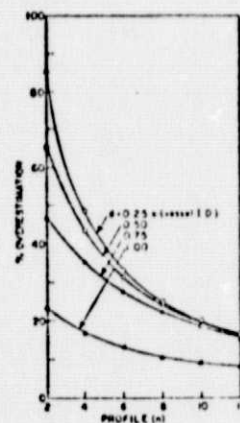


Fig. 1 Zero Crossing Overestimation of  $\bar{V}$  Within Vessel vs. Profile Number (parabolic,  $n = 2$ ; blunt,  $n = 12$ ) vs. Transducer Edge Length (d). Profile (n) was defined by  $\bar{V} = V_{max} (1 - r^n)$ .

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